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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
LAM, ANN Y	
ART UNIT	**PAPER NUMBER**
1641	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	12/20/2006	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/541,013	HENDERSON ET AL.	
	Examiner	Art Unit	
	Ann Y. Lam	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 November 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-17 and 28-42* is/are pending in the application.

4a) Of the above claim(s) *14-17 and 38-42* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-13 and 28-37* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *28 June 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *2/10/06, 7/10/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election without traverse of Group I, claims 1-13, in the reply filed on November 22, 2006 is acknowledged. Claims 14-17 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-10, 12, 13, 28-33, 36 and 37 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lal et al., "Multimodal Atomic Force Microscopy: Biological Imaging Using Atomic Force Microscopy Combined with Light Fluorescence and Confocal Microsopies and Electrophysiologic Recording", International Journal of Imaging Systems and Technology, Vol. 8, 293-300 (1997), in view of Peeters, 6,325,904.

Lal et al. disclose the invention substantially as claimed. More specifically, Lal et al. disclose a nanomanipulator having a tip mounted on a microcantilever which senses the interaction force between the molecules on the probe tip and sample surface (page 293, right column). Lal et al. teach that the apparatus can be used in cells and has subnanometer resolution (page 294, left column).

However, Lal et al. do not teach that the molecules on the probe tip are in an array (nanoarray).

Peeters however teach a cantilever having an array of electrodes with known receptors and position such that the position information can be used to detect attachment or binding (col. 6, lines 33-37). The detection can be for example fluorescence detection (col. 5, lines 61-65). While Lal et al. do not disclose that the molecules on the probe tip of the microcantilever are in a pattern (nanoarray), it nevertheless would have been obvious to one of ordinary skill in the art at the time the invention was made because Peeters teaches that probe molecules can be positioned on a cantilever in an array and that such an array provides the benefit of providing information relating to the binding of specific molecules known to be at a certain position.

As to claims 2 and 28, the array described above is considered a nanoarray because it is an array of molecules and on a microcantilever described as a nanomanipulator (Lal et al., page 293) and are spatially arranged in known locations as taught by Peeters.

As to claim 3, while Lal et al. disclose molecules on the probe tip for sensing interaction force between the molecules and a sample, Lal et al. do not specifically teach that the molecules are DNA. However, Peeters teaches that probe molecules on a cantilever can be DNA such that full DNA sequence can be reconstructed (col. 7, lines 54-61). It would have been obvious to one of ordinary skill in the art to provide DNA as the molecules on the Lal et al. microcantilever because Peeters teaches that such probe molecules provide the benefit of allowing full DNA sequence to be reconstructed.

As to the following claims, the limitations are disclosed by Lal et al. as follows.

As to claim 4, the structural elements of the microcantilever disclosed by Lal et al. which senses the interaction force are considered to be the claimed nanosensors operably connected to the array (page 293, right column).

As to claim 5, the probe is a microcantiliver (page 293, right column.)

As to claim 6, the Lal et al. microcantilever is considered to be a dual element probe because it has at least 2 molecules (page 293, right column).

As to claim 7, the Lal et al. microcantilever is considered to be a multielement probe because it has more than 1 molecule (page 293, right column).

As to claim 8, the probe is sized to interrogate a sample comprising a volume of about 50 femtoliters to about 10 microliters, because it can interrogate cells (page 294, left column).

As to claims 9 and 10, the apparatus comprises at least one microdisrupter, i.e., the tip, disposed on the probe (page 293, right column).

As to claim 12, the apparatus further comprises a molecular detection device operably connected to the probe (see photodetectors, page 293, right column).

As to claim 13, the molecular detection device is an electronic system, and is also considered an optical system because the deflection is sensed and converted to electrical signals by photodetectors (see page 293, right column).

As to claims 29 and 33, the probe is sized to interrogate a single cell (see page 293, disclosing that a microcantilever as a nanomanipulator for nanodissection and force-induced changes in molecular conformations). While Lal et al. do not disclose that the probe tip is smaller than a cell, Lal et al. nevertheless teach that it is a nanomanipulator for nanodissection, which thus suggest that it is in the nanometer range. Moreover, it has been held that where the general conditions of a claim are disclosed in the prior art, discovering the optimum or workable ranges involves only routine skill in the art. (see MPEP 2144,05 IIA, citing *In re Aller*, 105 USPQ 233.) In this case, Lal et al. disclose the general conditions of the claim, including that the microcantilever is very small, i.e., a nanomanipulator for nanodissection, and thus providing a microcantilever of a dimension that is smaller than a single cell is within an optimum or workable range.

As to claim 30, the probe is sized to interrogate a lysate of a single cell (page 293-294, disclosing the detection of molecules). It is noted that Applicants do not indicate how the probe interrogates a lysate, e.g., such as by piercing a cell.

As to claims 31 and 32, the probe is sized to interrogate a sub-cellular species of a cell, the subcellular species being a Golgi complex (page 293-294, disclosing the

detection of molecules). Applicants do not indicate how the probe is interrogating the sub-cellular species, such as by insertion into the subcellular species, and thus if the probe is sized to detect molecules, then it is considered to be sized to interrogate a subcellular species such as a Golgi complex.

As to claim 36, the molecules have a substance (i.e., molecules) that is considered to be reversibly attached because the molecules are capable of being detached, such as by physical force or by chemical means.

Claims 11, 34 and 35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lal et al., "Multimodal Atomic Force Microscopy: Biological Imaging Using Atomic Force Microscopy Combined with Light Fluorescence and Confocal Microsopies and Electrophysiologic Recording", International Journal of Imaging Systems and Technology, Vol. 8, 293-300 (1997), in view of Peeters, 6,325,904, and further in view of Yan et al., "A general microcantilever surface modification using a multilayer for biospecific recognition", Organic and Biomolecular Chemistry, available on-line (2002).

Lal et al. disclose the invention substantially as claimed (see above), except for the tip comprising an anti-wicking feature or hydrophobic.

However, Yan et al. teach that use of a hydrophobic coating (see third page) on a microcantilever which allow cantilevers to undergo bending due to molecular absorption to probes immobilized on the microcantilever by confining the adsorption to only one side of the cantilever so as to detect chemical and biological species that bind to the

probes (see introduction and also fifth and sixth page). Yan et al. teach that a bare gold coated silicon cantilever without the disclosed coating does not deflect upon exposure to the molecules of interest (see fifth page). It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the Lal et al. microcantilever such that the probe molecules are attached to the microcantilever using the coatings taught by Yan et al. because Yan et al. teach that the disclosed coatings provide the benefit of a means for immobilizing probes onto one side of a microcantilever for detection of molecular absorption, whereas a microcantilever without the coating may not deflect upon molecular absorption.

Claim 37 is rejected under 35 U.S.C. 103(a) as being unpatentable over Lal et al., "Multimodal Atomic Force Microscopy: Biological Imaging Using Atomic Force Microscopy Combined with Light Fluorescence and Confocal Microsopies and Electrophysiologic Recording", International Journal of Imaging Systems and Technology, Vol. 8, 293-300 (1997), in view of Peeters, 6,325,904, and further in view of Tamayo et al., "Chemical sensors and biosensors in liquid environment based on microcantilevers with amplified quality factor", Ultramicroscopy) (2001) 1-7.

Lal et al. in view of Peeters disclose the invention substantially as claimed (see above), except for the molecules being reversibly attached by a tether comprising a thermally sensitive tether.

Tamayo et al. teach that glutaraldehyde is used to covalently bind antibodies to a cantilever (page 3). The glutaraldehyde is considered to be a tether because it links the antibody molecules to the cantilever, and it is considered to be thermally sensitive because all molecules are sensitive to temperature. (It is noted that Applicants do not indicate as to how the tether responds to temperature). It would have been obvious to one of ordinary skill in the art at the time the invention was made to provide glutaraldehyde in the Lal et al. microcantilever because Tamayo et al. teach that glutaraldehyde provides the benefit of covalently binding molecules such as antibodies onto a cantilever, as would be desirable in the Lal et al. microcantilever in order to utilize the probe for sensing interaction between the molecules and a sample.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ann Y. Lam whose telephone number is 571-272-0822. The examiner can normally be reached on Mon.-Fri. 10-6:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on 571-272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

12/11/06

ANN YEN LAM
PATENT EXAMINER